Complete Summary

GUIDELINE TITLE

Practice advisory: the use of felbamate in the treatment of patients with intractable epilepsy. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society.

BIBLIOGRAPHIC SOURCE(S)

French J, Smith M, Faught E, Brown L. Practice advisory: the use of felbamate in the treatment of patients with intractable epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 1999 May 12;52(8):1540-5. [39 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Intractable epilepsy

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To determine the current role of felbamate for treatment of various types of epilepsy
- To provide guidelines to ensure maximum safety and effectiveness when the risk/benefit ratio is in favor of the use of felbamate

TARGET POPULATION

Patients with intractable epilepsy

INTERVENTIONS AND PRACTICES CONSIDERED

Felbamate therapy

MAJOR OUTCOMES CONSIDERED

- Frequency and severity of seizures
- Frequency of tonic and atonic seizures under felbamate therapy
- Incidence of side effects during adjunctive therapy and monotherapy with felbamate
- Felbamate interactions with other antiepileptic drugs
- Incidence of serious idiosyncratic events, including fatalities, with felbamate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A Medline search was performed for articles including the key word "felbamate." The search was restricted to English language only and human studies. The search identified 105 articles. The working group reviewed abstracts of all articles. Of the 105 articles, 54 were identified as relevant to the topics of efficacy, practice, treatment guidelines, and side effects.

In addition to the information obtained through the literature search, each panel member reviewed his or her assigned articles´ reference lists to determine whether any important articles were missed. Unpublished data on safety issues were also obtained from Carter Wallace Pharmaceuticals (Cranbury, New Jersey).

NUMBER OF SOURCE DOCUMENTS

54

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of evidence ratings

Class I: Well-designed, prospective, blinded, controlled studies

Class II: Well-designed clinical studies, such as case control, cohort studies, etc.

Class III: Evidence provided by expert opinion, nonrandomized historic controls, or case reports of one or more

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

All clinical studies were reviewed in their entirety, including case reports. Articles were excluded if they reviewed multiple drugs, discussed only mechanism of action, consisted of news reports, or summarized previous data without pro-viding new insight or opinion. Articles were rated as Class I, II, or III (see "Rating scheme for strength of the evidence" above). The 54 articles reviewed could be classified as follows:

Class I: Nine articles, seven related to efficacy and toxicity and two to pharmacokinetics.

Class II: One article related to brain levels of felbamate.

Class III: Forty-four articles including case reports, historic control studies, and reviews with expert opinion.

Studies were assessed for study design, toxicity (dose-dependent and idiosyncratic), and efficacy, including patient characteristics, seizure type being treated, and duration of treatment. Reviews were assessed to determine expert opinion on efficacy, toxicity, and the place of felbamate in the treatment of various seizure types.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Definitions for Strength of Recommendations:

Standard: A principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical question, or overwhelming Class II evidence when circumstances preclude randomized clinical trials).

Guideline: A recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence).

Practice option: A strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).

Practice Advisory: A practice recommendation for emerging and/or newly approved therapies or technologies based on evidence from at least one Class I study. The evidence may demonstrate only a modest statistical effect or limited (partial) clinical response, or significant cost-benefit questions may exist. Substantial (or potential) disagreement among practitioners or between payers and practitioners may exist.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Drafts of the guideline were reviewed by numerous individuals, American Academy of Neurology sections, and organizations, including the American Epilepsy Society, the Epilepsy Foundation of America, and the Child Neurology Society.

The guideline was approved by the American Academy of Neurology Quality Standards Subcommittee October 17, 1998, by the Practice Committee on January 23, 1999, and by the Executive Board of the American Academy of Neurology on February 27, 1999.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence ratings, I-III, and the definitions (Standard, Guideline, Practice Option, Practice Advisory) are defined at the end of the "Major Recommendations" field.

The guideline developers recognize the potential serious side effects that may exceed those of primary antiepileptic drugs; however, felbamate can be an effective antiepileptic drug and has important advantages if used in certain patient populations.

The following recommendations were made as an advisory:

A. Patients for whom risk/benefit ratio supports use because there is Class I evidence for benefit.
    1. Lennox–Gastaut patients over age 4 unresponsive to primary antiepileptic drugs.
    2. Intractable partial seizures in patients over 18 years of age who have failed standard antiepileptic drugs at therapeutic levels (monotherapy: data indicate a better risk/benefit ratio for felbamate used as monotherapy).
    3. Patients on felbamate more than 18 months.
B. Patients for whom the current risk/benefit assessment does not support the use of felbamate:
    1. New onset epilepsy in adults or children
    2. Patients who have experienced significant prior hematologic adverse events
    3. Patients in whom follow-up and compliance will not allow careful monitoring
    4. Patients unable to discuss risks/benefits (i.e., with mental retardation, developmental disability) and for whom no parent or legal guardian is available to provide consent
C. Patients in whom risk/benefit ratio is unclear and based on case reports and expert opinion (Class III) only, but under certain circumstances depending on the nature and severity of the patient´s seizure disorder, felbamate use may be appropriate:
    1. Children with intractable partial epilepsy
    2. Other generalized epilepsies unresponsive to primary agents
    3. Patients who experience unacceptable sedative or cognitive side effects with traditional antiepileptic drugs.
    4. Lennox–Gastaut syndrome under age 4 unresponsive to other antiepileptic drugs.

Risk management

1. As therapy continues, risk/benefit ratio should be constantly assessed.
2. Patients should be educated as to early signs of potentially serious hepatic and hematopoetic side effects. These signs are: easy bruising, prolonged excessive bleeding, change in skin color, fatigue, fever, change in stool color, change in the color of the whites of the eye.
3. Laboratory monitoring has not been proved efficacious, but the manufacturer (Carter-Wallace), in conjunction with the U.S. Food and Drug Administration (FDA), suggests liver function tests at baseline and every 1 to 2 weeks for the first year of therapy, and also notes that complete blood count may identify

hematologic changes before symptoms occur. There is no evidence that such monitoring will prevent adverse outcomes. After the first year, the risk of aplastic anemia drops and the need for ongoing laboratory screening is even less clear.

4. Even though individual clinical practice may vary, patients should be advised of the manufacturer´s recommendations.

Definitions:

Quality of evidence ratings

Class I: Well-designed, prospective, blinded, controlled studies.

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Definitions:

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on a review of the literature. The type of supporting evidence is identified and graded for the use of felbamate in the

treatment of patients with intractable epilepsy (See "Major Recommendations" field).

Both Class I and Class III evidence was found to support recommendations for the efficacy of felbamate in various types of epilepsy. Class I evidence was found for risks for side effects, and Class III evidence only was found for serious risks of felbamate.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of felbamate in treatment of various types of epilepsy, taking into account the risks and benefits of treatment

Subgroups Most Likely to Benefit:

- Adults and children over age 4 with Lennox-Gastaut syndrome
- Adults (over age 18) with intractable partial seizures

POTENTIAL HARMS

- Dose-limiting side effects
    - Nausea, abdominal distress, anorexia, insomnia, fatigue, dizziness, ataxia, cognitive impairment, and weight loss
- Drug interactions (when used as adjunct therapy), some potentially causing toxicity
- Serious (sometimes fatal) idiosyncratic events
    - Serious rash, aplastic anemia, and hepatic failure
    - Stevens-Johnson syndrome and toxic epidermal necrolysis

Subgroups Most Likely to be Harmed:

Patients who are being treated with adjunctive therapy or polytherapy, including phenytoin, valproate, or carbamazepine

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

Future research should be performed to determine the following information:

1. Potential risk factors that may be associated with the development of serious adverse events with felbamate use
2. Potential for diagnostic testing that would predict susceptibility to serious adverse events

The guideline developers recommend that physicians prescribing felbamate register their patients in the Felbatol Registry so that these goals may be accomplished. The registry can be contacted at: Felbatol Registry Program, Wallace Laboratories Data Management Services, PO Box 1001, Half-Acre Road, Cranbury, New Jersey 08512-0181.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 May

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society
American Epilepsy Society - Disease Specific Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Quality Standards Subcommittee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

American Academy of Neurology Quality Standards Subcommittee Members: Gary Franklin, MD, MPH (Co-chair); Catherine A. Zahn, MD (Co-chair); Milton Alter, MD, PhD; Stephen Ashwal, MD; John Calverley, MD; Richard Dubinsky, MD; Jacqueline French, MD; Michael K. Greenberg, MD; Gary Gronseth, MD; Deborah Hirtz, MD; Robert G. Miller, MD; and James Stevens, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Drs French and Faught have received research support from Carter–Wallace Pharmaceuticals. Drs French, Faught, and Smith are past members of a speakers´ bureau supported by Carter– Wallace. Dr. Faught has been a consultant for Carter–Wallace.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

AVAILABILITY OF COMPANION DOCUMENTS

- Practice statement definitions. St. Paul (MN): American Academy of Neurology.
- Practice statement development. St. Paul (MN): American Academy of Neurology.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on February 12, 2002. The information was verified by the guideline developer as of March 29, 2002.

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